



Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy (Last updated December 12, 2019; last reviewed December 12, 2019)

Panel's Recommendations

- Women living with HIV who are receiving antiretroviral therapy (ART) and who present for pregnancy care should continue their ART during pregnancy, provided that the regimen is tolerated, safe, and effective in suppressing viral replication (defined as a regimen that maintains an HIV viral load less than lower limits of detection of the assay) (AII).
- Women who present during pregnancy on drugs that are not recommended for use because of toxicity (e.g., stavudine, didanosine) should stop taking these drugs and be switched to other antiretroviral (ARV) drugs that are recommended for use in pregnancy (AIII). See [Table 5](#) for more information.
- For pregnant women who are receiving dolutegravir (DTG) and present to care during pregnancy, providers should counsel these women about the risks and benefits of continuing DTG or switching to another ARV regimen (AIII). In most cases, the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission recommends **continuation** of DTG (AIII).
- There are no data on the use of two-drug regimens during pregnancy (e.g., DTG plus lamivudine, DTG plus rilpivirine); women who present to care on one of these regimens should switch regimens or add additional ARV agents to these regimens.
- Regimens that contain atazanavir/cobicistat, darunavir/cobicistat, or elvitegravir/cobicistat are associated with pharmacokinetic changes and an increased risk of virologic failure in the second and third trimesters of pregnancy (see [Table 4](#) and [Table 5](#)); when a pregnant woman presents to care on one of these regimens, providers should consider switching her to a more effective regimen that is recommended for use in pregnant women (BIII). If one of these regimens is continued, absorption should be optimized, and viral load should be monitored frequently (i.e., every 1–2 months).
- If an ARV regimen is altered during pregnancy, drugs in the new regimen should include ARV drugs that are recommended for use in pregnancy (see [Table 4](#) and [Table 5](#) (BIII), and more frequent virologic monitoring is warranted (CIII).
- ARV drug-resistance testing should be performed to assist the selection of active drugs when changing ARV regimens in pregnant women who are experiencing virologic failure on ART and who have HIV RNA levels >500 copies/mL to 1,000 copies/mL (AII). In individuals who have HIV RNA levels >500 copies/mL but <1,000 copies/mL, testing may be unsuccessful but should still be considered (BII). See [Lack of Viral Suppression](#) for more information.
- Clinicians should discuss future reproductive plans and timing as well as the risks and benefits of conceiving on specific ARV medications and use of appropriate contraceptive options to prevent unintended pregnancy (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Women who are taking antiretroviral therapy (ART) for HIV infection should continue their ART regimen during pregnancy, provided it is well tolerated, safe, and effective in suppressing viral replication. Discontinuing or altering therapy could cause an increase in viral load, leading to disease progression, a decline in immune status, and an increased risk of perinatal HIV transmission.¹ Maintenance of viral suppression is paramount for both maternal health and the prevention of perinatal transmission. However, a change in ART may be indicated or considered in specific circumstances.

Women who present during pregnancy on drugs that are not recommended for use because of toxicity (e.g., stavudine, didanosine) should stop taking these drugs and switch to other antiretroviral (ARV) drugs that are recommended for use in pregnancy (see [Table 4](#) and [Table 5](#)).

Dolutegravir (DTG) exposure at the time of conception has been associated with a small increase in the risk of neural tube defects (NTDs) in infants.^{2,3} Pregnant women who present to care on DTG-based regimens should receive counseling about the benefits and risks of continuing to use DTG or switching regimens. The neural tube closes by approximately 4 weeks post-conception, or approximately 6 weeks after the last menstrual period in women with regular menses. The Tsepamo study in Botswana reported five NTDs among infants born to women who were receiving DTG at the time of conception. One of the observed NTDs may have been a defect that can occur during the first trimester, but after the neural tube has closed (a post-neurulation event). However, in cases where a woman conceives while taking DTG, the clinician and patient

must discuss whether the patient should continue using DTG or switch to another ARV regimen.

Women often detect pregnancy and present to care between 6 and 14 weeks of gestational age. In these situations, providers should review the following considerations with their patients:

- Most NTDs occur before the neural tube closes at 4 weeks post-conception, approximately 6 weeks post-last menstrual period. After 6 weeks gestation, the additional risk of NTDs developing is thought to be much less likely;
- There is a background risk of NTDs regardless of ART regimen or HIV status (in the United States, the background risk of NTDs in the general population is 0.07%);⁴ and
- Changes in ARV regimens can lead to viral rebound, which may increase the risk of perinatal HIV transmission and may reduce future ARV drug options due to the development of resistance.

A careful consideration of these risks and benefits will allow patients and providers to reach individualized decisions about whether a patient should continue using DTG or switch to a different ARV regimen during the pregnancy. In most cases, the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (the Panel) recommends **continuation** of DTG. There are no data on the use of two-drug regimens in pregnancy (e.g., DTG plus lamivudine, DTG plus rilpivirine [RPV]); women who present to care on one of these regimens should switch regimens or add additional ARV agents to these regimens.

It is important to weigh the available data about the risks of using DTG against what is known (or not known) about the risks of NTDs when using other *Preferred* and *Alternative* agents. These agents include atazanavir/ritonavir, darunavir/ritonavir, and raltegravir (*Preferred*), and lopinavir/ritonavir, EFV, RPV (*Alternative*). Of these, systematic birth surveillance data are available only for EFV. In addition, other adverse pregnancy outcomes are more common than NTDs and should also be considered. The use of protease inhibitors has been associated with an increased risk of preterm birth, which may lead to increases in infant morbidity and mortality (see [Combination Antiretroviral Drug Regimens and Maternal and Neonatal Outcomes](#)). While DTG carries a higher risk of NTDs than EFV, the two drugs have similar rates of other adverse pregnancy outcomes. However, tolerability and long-term viral suppression may be enhanced with DTG-based regimens.^{5,6}

When a pregnant woman presents to care on a regimen that contains atazanavir/cobicistat, darunavir/cobicistat, or elvitegravir/cobicistat (EVG/c), providers should consider switching her to a more effective regimen that is recommended for use in pregnant women. The use of these regimens is associated with pharmacokinetic changes and an increased risk of virologic failure in the second and third trimesters of pregnancy (see [Table 4](#) and [Table 5](#)).⁷⁻⁹ A recent multicenter, retrospective study of 134 pregnant women with HIV who received elvitegravir (EVG)-containing ART at any time during pregnancy reported that 81.3% of study participants had viral suppression at delivery (HIV RNA <40 copies/mL); among 68 women who initiated EVG before pregnancy and continued receiving EVG through delivery, the rate of viral suppression at delivery was 88.2%. The perinatal HIV transmission rate was 0.8% in this study.¹⁰ If one of these regimens is continued, absorption should be optimized by taking the drugs with food. Women who are taking regimens that include EVG/c should take ARV drugs and prenatal vitamins ≥ 2 hours apart. In addition, viral load should be monitored more frequently in patients taking cobicistat boosted regimens (e.g., every 1–2 months) (see [Monitoring of the Woman and Fetus During Pregnancy](#)).¹¹ Lack of virologic suppression on subsequent testing indicates a need for a regimen change, and a woman may need a scheduled cesarean delivery if the lack of suppression is detected late in pregnancy.

Although PK data indicate that RPV plasma concentration is reduced during the second and third trimesters of pregnancy, the reduction is less than the reductions seen with the cobicistat-containing regimens described above, and most women will have adequate exposure. Standard RPV dosing is recommended, and viral load should be monitored frequently (e.g., every 1–2 months; see [Recommendations for Use of Antiretroviral Drugs During Pregnancy](#)).

As newer, highly effective ARV drugs are approved by the Food and Drug Administration, women with

HIV may present for prenatal care on ART regimens that include ARV drugs for which there is a lack of significant experience in pregnancy and limited PK and safety data. If questions arise about specific drugs in an ART regimen, providers are encouraged to consult with an HIV perinatal specialist before discontinuing or altering a fully suppressive regimen that is well tolerated. In addition, more frequent virologic monitoring is warranted when an ARV regimen is altered during pregnancy. Because little is known about the use of newly approved drugs in pregnancy, providers should make every effort to report all ART exposures in pregnant women to the [Antiretroviral Pregnancy Registry](#).

Women with HIV who are on ART and who present for care during the first trimester should be counseled regarding the benefits and potential risks of receiving ARV drugs during this period. Providers should emphasize that continuing an effective ARV regimen is recommended. Nonhuman primate data and retrospective case reports have raised concerns about an association between EFV use during the first trimester and an increased risk of NTDs in infants (for more details, see [Efavirenz](#)). However, a meta-analysis that included data on 2,026 women with first-trimester EFV exposure from 21 prospective studies did not find an increased relative risk (RR) of overall birth defects in infants born to women who received EFV-based regimens compared to women who received regimens that did not include EFV (RR 0.78; 95% confidence interval, 0.56–1.08).¹² A recent multicohort analysis of seven observational studies across 13 European countries and Thailand included 24,963 live births to women with HIV. This study evaluated the incidence of birth defects among infants who had been exposed to either EFV-based ART (n = 1,200) or ART that did not contain EFV (n = 7,537) at the time of conception or during the first trimester; the study also evaluated infants who were not exposed to ART (n = 16,226) at the time of conception or during the first trimester. There was no difference in the prevalence of birth defects among infants in these three groups.¹³ The Panel recommends continuing to use EFV in pregnant women who are receiving EFV-based ART, provided that the ARV regimen is well tolerated and results in virologic suppression.

Resistance testing should be performed when considering altering an ARV regimen in a pregnant woman who is experiencing virologic failure and who has HIV RNA levels >1,000 copies/mL. In individuals who have HIV RNA levels >500 copies/mL but <1,000 copies/mL, testing may be unsuccessful, but it still should be considered. The results can be used to select a new regimen with a greater likelihood of suppressing viral replication to undetectable levels.

During and after pregnancy, clinicians should discuss future reproductive plans and timing as well as the risks and benefits of conceiving on specific ARV medications and contraceptive options to prevent unintended pregnancy (see [Preconception Counseling and Care for Women of Childbearing Age Living with HIV](#)).

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